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Occupational allergic contact dermatitis and patch test results of leather workers at two Indonesian tanneries

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Summary

Background. Tannery workers are at considerable risk of developing occupational contact dermatitis. Occupational skin diseases in tannery workers in newly industrialized countries have been reported, but neither the prevalence of occupational allergic contact dermatitis nor the skin-sensitizing agents were specifically examined in those studies.

Objectives. To assess the prevalence of occupational allergic contact dermatitis in Indonesian tanneries, identify the causative allergens, and propose a tannery work series of patch test allergens.

Patients/methods. A cross-sectional study in all workers at two Indonesian tanneries was performed to assess the prevalence of occupational contact dermatitis via a questionnaire-based interview and skin examination. Workers with occupational contact dermatitis were patch tested to identify the causative allergens.

Results. Occupational contact dermatitis was suspected in 77 (16%) of the 472 workers. Thirteen (3%) of these 472 workers were confirmed to have occupational allergic contact dermatitis. Potassium dichromate (9.2%), *N*,*N*-diphenylguanidine (5.3%), benzidine (3.9%) and sodium metabisulfite (2.6%) were found to be the occupationally relevant sensitizers.

Conclusions. The sensitization pattern showed some differences from the data in studies reported from other newly industrial countries. We compiled a 'tannery work series' of allergens for patch testing. A number of these allergens may also be considered for patch testing in patients with (leather) shoe dermatitis.

Key words: occupational allergic contact dermatitis; occupational contact dermatitis; patch test; tannery workers.

Tanning is the process of converting animal hides into leather, a product that does not easily decompose. Tanning has been in use since 7000 BC, and is considered to be a noxious and smelly trade, which had to be confined to the outskirts of town in the poor areas. The chemicals used in leather production are intended to alter the structure of the animal hide, and may have the same effect on the worker's skin. Many of these chemicals are considered to be potential sensitizers. Tannery workers, who are frequently exposed to these chemicals for prolonged periods, are at considerable risk of developing occupational allergic contact dermatitis (1, 2).

Occupational skin diseases in the leather industry have rarely been reported over the last decades, despite their high risk potential. This lack of reporting may have been caused by the outsourcing of leather production to newly industrialized countries, which do not have a comprehensive occupational disease registry and properly conducted occupational dermatological surveys, such as those in industrialized Western countries (3). The

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relocation of hazardous industries to developing countries is driven by economic considerations – high levels of unemployment, a cheaper labour force, lack of regulation, and poor enforcement of any existing regulations – that make certain countries highly profitable for business ventures (3, 4). Since the 1980s, many Western countries have prohibited the use of certain chemicals for tanning (5), and this has led companies to outsource tannery work to the newly industrial countries.

Occupational allergic contact dermatitis in tannery workers was often seen in Western countries decades ago, prior to the introduction of the strict regulations on occupational exposure (2, 6). Recently published data on occupational skin diseases in tannery workers were reported from newly industrial countries such as India and Argentina, but the actual prevalence of occupational allergic contact dermatitis and the skin sensitization to tannery allergens were not investigated (7–9). Outsourcing tannery work to newly industrial countries may influence the risk of developing occupational allergic contact dermatitis in workers in this industry.

In a previous report, we presented a detailed overview of the exposure to the putative source of occupational irritant and sensitizing agents at tanneries, and described the prevalence of occupational skin diseases in workers (10).

The purpose of this study was to (i) assess the prevalence of occupational allergic contact dermatitis in a population of tannery workers in a newly industrialized country, (ii) identify the causative allergens, and (iii) propose a tannery works series of patch test allergens.

Materials and Methods

We conducted a cross-sectional study to assess the prevalence of occupational allergic contact dermatitis at two tanneries in Java, Indonesia between March and December 2009. These tanneries represent a plant with high mechanization and a plant with medium mechanization, according to the list provided by the Indonesian Centre for Leather (10). All employees engaged in the production process and thus exposed to potentially hazardous chemicals were included in the study.

Structured interviews

The interviews were conducted with the Indonesian translation of the Nordic Occupational Skin Questionnaire (NOSQ-2002/LONG). The questionnaire was translated, adapted and modified for specific circumstances at the tanneries following the guidelines from the Nordic Occupational Skin Questionnaire Group (11–13). Interviews were carried out to obtain information on the locations and morphological aspects of the skin diseases, and the exposure to relevant allergens in the workplace.

Dermatological examination and patch testing

The skin of all workers was examined by a team of dermatologists supervised by a dermatologist with additional training in contact and occupational dermatitis within a period of 5 weeks. Patch tests were performed in 63 of 77 tannery workers with current dermatitis and a history suggestive of occupational contact dermatitis, and in 108 tannery workers without skin disease as controls.

We used allergens from the European baseline series, from the shoe series (Chemotechnique Diagnostics®, Vellinge, Sweden), and additional allergens specific for tannery work. These additional allergens were identified on the basis of the previously reported inventory of potential allergens and exposure assessment at these tanneries (10). We used analytical grade chemicals for non-allergen manufacturer substances. We prepared the sodium metabisulfite patch test material in our laboratory with petrolatum as a vehicle to formulate a more stabile preparation. A list of specific allergens to which the tannery workers were exposed and that were used for patch testing is shown in Table 1.

The patch test procedures were performed on the upper back of the workers with Finn Chambers® (Epitest Ltd., Helsinki, Finland) mounted on Scanpor® tape (Alpharma AS, Norgersplaster Facility, Norway). The applied patch tests were reinforced with extra tape stuck at the margin and covering the chamber area: this procedure is recommended in hot climates to avoid detachment of the strips (14). After 48 hr of occlusion, we removed the Finn Chambers®, and we read the patch test result on days 2, 4, and 7, as recommended by the International Contact Dermatitis Research Group (14, 15).

Diagnostic criteria for occupational allergic contact dermatitis

The diagnostic criteria for occupational allergic contact dermatitis in this study were based on the information from three sources: workplace observation, questionnaire, and dermatological examination, including patch test results.

The diagnosis of occupational allergic contact dermatitis was established in cases meeting the following criteria (11, 16, 17):

(1) Confirmed as a case of occupation-related contact dermatitis
(2) Exposure to the relevant occupational allergens

Table 1. Sensitizers to which the tannery workers were exposed

Work area and process	Chemicals used and identified as sensitizer (source)	Concentration and vehicle	CAS number
Preparation of the hides in the beam house			
Preservation	Sodium *N*-methyldithiocarbamate[a] (Supelco)	0.03% pet.	6734-80-1
	2-n-Octyl-4-isothiazolin-3-one[b]	0.1% pet.	213-34
	MCI/MI[b]	0.02% aqua	55965-84-9
Soaking	Sodium *N*-methyldithiocarbamate[a] (Supelco)	0.03% pet.	6734-80-1
Green fleshing	—	—	—
Liming and watering	—	—	—
Fleshing	—	—	—
Splitting	—	—	—
Pre-tanning section			
De-liming	Hydrogen peroxide[a](Sigma-Aldrich)	3.0% aqua	7722-84-1
Bating	2-(2-bromoethyl) Benzaldehyde[a] (Aldrich)	2.0% pet.	22901-09-3
Pickling	Sodium formate[a] (Sigma Aldrich)	2.0% glycerol	141-53-7
	Sodium metabisulfite[a] (Sigma Aldrich)	1.0% pet.	7681-57-4
Tanning section			
Tanning	Potassium dichromate[b]	0.5% pet.	7778-50-9
	2-Mercaptobenzothiazole[b]	2.0% pet.	149-30-4
	Sodium *N*-methyldithiocarbamate[a](Supelco)	0.03 % pet.	6734-80-1
	Formaldehyde[b]	1.0% aqua	50-00-0
	Polyethyl acrylate[a] (Aldrich)	5.0% pet.	9003-32-1
	Glycine[a] (Sigma)	2.0% aqua	56-40-6
	Chlorobenzene[a] (Sigma Aldrich)	5.0% olive oil	108-90-7
	Oxalic acid[a] (Sigma Aldrich)	0.1% aqua	144-62-7
	Glutaraldehyde[b]	0.2% pet.	111-30-8
	2-(thiocyanomethylthio) Benzothiazole[a]	0.2% pet.	21564-17-0
Sammying	—	—	—
Shaving	—	—	—
Finishing			
Fat liquoring	—	—	—
Dyeing	Disperse Orange 3[b] (CI 11005)	1.0% pet.	730-40-5
	Acid Yellow 36[b] (CI 13065)	1.0% pet.	587-98-4
	N-Isopropyl-*N*-phenyl-4-phenylenediamine[b]	0.1% pet.	101-72-4
	Hydrogen peroxide[a]	3.0% aqua	7722-84-1
	Benzidine[a] (Sigma)	1.0% pet.	92-87-5
Finishing	Epoxy resin (adhesive)[b]	1.0% pet.	28064-14-4
	Polyethylacrylate[a] (Aldrich)	5.0% pet.	9003-32-1
	Formaldehyde[b]	1.0% aqua	50-00-0
	Colophonium (surface coating)[b]	20.0% pet.	8050-09-7
	4-tert-Butylphenol formaldehyde resin[b]	1.0% pet.	98-54-4

MCI/MI, methylchloroisothiazolinone/methylisothiazolinone.
[a]Additional allergens for tannery work.
[b]Present in the standard shoe series of Chemotechnique Diagnostics®.

(3) Confirmed Type 4 sensitization to the relevant occupational allergens
(4) Exposure confirmed as a cause or as an important aggravating factor in the development of the skin diseases.

To confirm a case of occupationally relevant contact dermatitis, we used a combination of structured questionnaire-based interview and skin examination by dermatologists.

Results

Characteristics of the studied workers

All 472 workers (112 females and 360 males) employed in the production process at the two tanneries were included

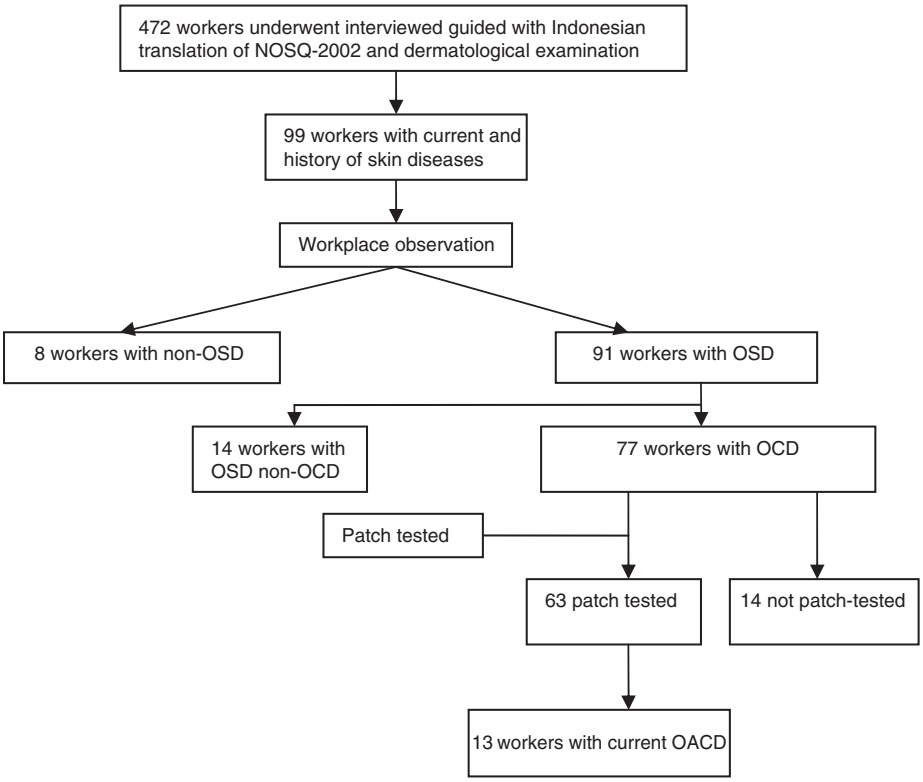

Fig. 1. Flowchart of the 472 workers. OACD, occupational allergic contact dermatitis; OCD, occupational contact dermatitis; OSD, occupational skin disease.

in the study. Their mean age was 36 years, and they had a mean duration of employment of 6 years and mean working hours per week of 47 hr. Twenty-one workers (4%) had a history of childhood eczema, 96 workers (20%) had a history of atopic respiratory disease, and 101 workers (22%) had atopic skin diathesis.

Development of specific tannery patch test series

On the basis of the previously reported workplace observations and the list of allergens that were identified at these tanneries (18), a literature search was performed to define a preferred vehicle and preferred concentrations of patch test allergens that were not commercially available (Table 1) (19).

Dermatological examination and patch test results

Occupational contact dermatitis was suspected in 77 (16%) of the 472 workers. Patch tests were performed in 63 of these workers; 13 (3%) had a positive patch test reaction to one or more of the tannery allergens and were diagnosed having occupational allergic contact dermatitis (Fig. 1).

Table 2. Location of the skin complaints in workers with current and past occupational contact dermatitis

Location of the skin lesion	Number of workers[a]
Hand wrist/forearm	68
Face/neck	5
Lower extremities	24
Trunk	52

[a]More than one area can be involved in a worker.

Locations of skin lesions in workers with occupational contact dermatitis

The locations of the skin lesions in the 77 workers with occupational contact dermatitis are shown in Table 2. The hands and the wrist/forearms were the areas generally affected by the occupation-related skin disease. In this population, we found that more than half of workers had involvement of the face/neck, the lower extremities, and the trunk.

Sensitization

A list of the relevant allergens to which sensitizations were seen is shown in Table 3. We found sensitization to 15

Table 3. Sensitization in workers with occupational allergic contact dermatitis

Allergen	Number of workers with positive patch test reaction (n = 76) (%)	Source of exposure
Potassium dichromate	7 (9.2)	Tanning
N,*N*-Diphenylguanidine	4 (5.3)	Synthetic rubber gloves
4-tert-Butylphenol formaldehyde resin	1 (1.3)	Surface coating and varnishing
p-Phenylenediamine base	1 (1.3)	Intermediate in dyeing and finishing
Colophonium	1 (1.3)	Surface coating in finishing stage
Formaldehyde	1 (1.3)	Tanning
2-Mercaptobenzothiazole	1 (1.3)	Tanning
Epoxy resin	1 (1.3)	Finishing
MCI/MI	1 (1.3)	Preparation of the hides
2-n-Octyl-4-isothiazolin-3-one	1 (1.3)	Preparation of the hides
Benzidine (1% pet.)	3 (3.9)	Finishing/dyeing
Sodium metabisulfite	2 (2.6)	Pickling
Sodium formate (2% glycerol)	1 (1.3)	Pickling
Chlorobenzene (5% olive oil)	1 (1.3)	Tanning
Oxalic acid	1 (1.3)	Tanning

MCI/MI, methylchloroisothiazolinone/methylisothiazolinone; n, number of workers with current and history of occupational contact dermatitis who were patch-tested.

allergens that were relevant in tannery work. The most frequent sensitizers observed were potassium dichromate (7 workers), *N*,*N*-diphenylguanidine (4 workers), benzidine (3 workers), and sodium metabisulfite (2 workers).

Discussion

The prevalence of 16% for occupational contact dermatitis in this group of exposed workers at the two Indonesian tanneries is lower than the prevalence of contact dermatitis in Korean tanneries (26.4%) (20), but higher than the 2.6% in a study at Indian tanneries (21). In addition to the differences in working conditions, the range of prevalences may be explained by the differences in the definition of cases, period of screening, and data collection (18). The prevalence of occupational contact dermatitis in our population is similar to those reported for wet-work exposure in Western populations (22–24). The prevalence of occupational allergic contact dermatitis might be higher, as we were not able to patch test all workers with occupational contact dermatitis: 14 of the workers were not patch tested, for different reasons, such as reluctance to be patch tested, moving to another factory, and not turning up for the examination. Workers in newly industrial countries, where there is job uncertainty and a lack of social security, may be reluctant to be diagnosed with occupational allergic contact dermatitis. Nevertheless, we consider the prevalence of occupational skin disease (21%), occupational contact dermatitis (16.3%) and occupational allergic contact dermatitis (3%) in this population of tannery workers to be high. These occupational diseases could probably be prevented with adequate and easily implemented measures (10).

In many cross-sectional studies on occupational diseases, the results may be affected by a healthy-worker survivor effect. Workers who experience occupational health problems are more likely to leave high-exposure jobs, either by ending employment or being transferred to another department (25). Observations and in-depth interviews with workers and management support this.

The hands and the wrist/forearms were the most common areas (68%) involved in this study. However, in this study, occupational contact dermatitis also affected other part of the body, such as the trunk, the lower extremities, and the face/neck, in >50% of the workers. A possible explanation for these typical disease locations is the use of inappropriate personal protective equipment: working without a shirt, wearing shorts, and using wet and contaminated aprons or boots (18).

Among the 63 workers who were patch tested, we found sensitizations to 15 allergens in 13 different workers. Determining the occupational relevance of sensitization is essential for the diagnosis of occupational allergic contact dermatitis. Potassium dichromate (9.2%), *N*,*N*-diphenylguanidine (5.3%), benzidine (3.9%) and sodium metabisulfite (2.6%) were found to be occupationally relevant sensitizers at these tanneries.

The results of our study showed some differences from data reported from an outpatient clinic-based study in a Western country and epidemiological studies in other newly industrialized countries. Data from a compilation of patch test results were reported in Germany and Sweden (2). Over the years 1960–1969, 12% of the Swedish male workers with chromate allergy were engaged in tannery work (6). Studies at outpatient clinics in Germany showed that the causative allergens for occupational allergic contact dermatitis in tannery workers were dichromate (3.2%), formaldehyde (1.3%), leather dyes (1.3%), and tanning agents (0.3%) (26). This study was performed before most of the tannery work was outsourced to newly industrialized countries. Sensitizations were assessed in Korean and Argentinian tannery workers. In a study of 310 Korean tannery workers, 10 of

22 workers who underwent patch testing had positive patch test reactions to carba mix, ammoniated mercury, gold sodium thiosulfate, formaldehyde, potassium dichromate, nickel sulfate, and mercaptobenzothiazole (20) In Argentina, 187 workers had positive patch test reactions to potassium dichromate, mercaptobenzothiazole, and hexachlorophene (8).

It is interesting to note that we found sensitizations to sodium metabisulfite (2.6%), benzidine (3.9%), and *N*,*N*-diphenylguanidine (5.3%). The prevalence of positive patch test reactions to sodium metabisulfite in some occupational dermatology clinics is between 3.4% (27) and 4.1% (28), but occupational relevance is found in only 1.9% (27) and 0.9% (28) patients. Occupationally relevant exposures were found in bakers, caterers, rubber manufacturers, and textile dyes (27–29). The leather industry is one of the occupational sources of sodium metabisulfite, which is used as an acidifying agent in the tanning process (30). In this study, 2 workers had relevant exposure to sodium metabisulfite.

We noted that one of the tanneries used benzidine-based dyes, and we found that 3.9% of workers were sensitized to benzidine. Reports on benzidine sensitization are scarce: one was published three decades ago, from a study of 4600 patients who were patch tested in Spain between 1973 and 1977 (31). Grimalt et al. (1981) performed histological studies of patch test reactions to confirm the allergic nature of the reactions (32). Benzidine-based dyes were banned in 1978 in many countries, because of their carcinogenic effect (5, 33). This explains why there are no recent reports on benzidine sensitization. Nevertheless, the continued demand by the textile and leather industry for benzidine-based dyes opened marketing opportunities in newly industrialized countries with less concern for workers and environmental safety (5). The detection of ongoing exposure and sensitization to benzidine in these tanneries can be seen as a sign that outsourced tannery work needs better enforcement of existing regulations.

In this population, 5.3% of the workers with skin complaints and 4% (4 of 108) of the workers without skin problems were sensitized to *N*,*N*-diphenylguanidine. Interpretation of *N*,*N*-diphenylguanidine patch test results remains difficult, as results from the Information Network of Departments of Dermatology for 1995–2001 indicate that most of the weak positive reactions to diphenylguanidine are probably irritant reactions (34). Although the assessment of patch test results was based on the visual inspection by a trained dermatologist, we cannot completely exclude the possibility of irritant reactions. The source of exposure to *N*,*N*-diphenylguanidine of tannery workers in this study was probably synthetic rubber gloves.

In our study, we were able to perform a careful identification of the possible sensitizers to which tannery workers were exposed. We assembled a 'tannery work series' of allergens for patch testing. A number of these allergens, for example sodium *N*-methyldithiocarbamate, sodium formate, sodium metabisulfite, and benzidine, may also be considered for patch tests in patients with (leather) shoe dermatitis as an addition to the commonly used shoe series.

In this study, we did not undertake random sampling when choosing the tanneries. The paucity of occupational health information in this industry made random sampling impossible. In order to obtain an overview of the working conditions at the Indonesian tanneries, we chose one tannery that represented two different types according to the list provided by the Indonesian Centre for Leather (10). Further study with a larger population and random sampling is needed to clearly establish the occupational health risk in such outsourced industries.

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